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Report

Abnormal fMRI Adaptation to Unfamiliar Faces in a Case of Developmental Prosopamnesia

Mark A. Williams,[1,2,*] Nadja Berberovic,[3] and Jason B. Mattingley[4]
[1] Macquarie Centre for Cognitive Science
Macquarie University
Sydney, NSW 2109
Australia
[2] McGovern Institute for Brain Research
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
[3] School of Psychological Science
La Trobe University
Bundoora, Victoria 3086
Australia
[4] Queensland Brain Institute and School of Psychology
University of Queensland
Queensland 4072
Australia

Summary

In rare cases, damage to the temporal lobe causes a selective impairment in the ability to learn new faces, a condition known as prosopamnesia [1]. Here we present the case of an individual with prosopamnesia in the *absence* of any acquired structural lesion. "C" shows intact processing of simple and complex nonface objects, but her ability to learn new faces is severely impaired. We used a neural marker of perceptual learning known as repetition suppression to examine functioning within C's fusiform face area (FFA), a region of cortex involved in face perception [2]. For comparison, we examined repetition suppression in the scene-selective parahippocampal place area (PPA) [3]. As expected, normal controls showed significant region-specific attenuation of neural activity across repetitions of each stimulus class. C also showed normal attenuation within the PPA to familiar and unfamiliar scenes, and within the FFA to familiar faces. Critically, however, she failed to show any adaptive change within the FFA for repeated *unfamiliar* faces, despite a face-specific blood-oxygen-dependent response (BOLD) response in her FFA during viewing of face stimuli. Our findings suggest that in developmental prosopamnesia, the FFA cannot maintain stable representations of new faces for subsequent recall or recognition.

Results and Discussion

C is a 28-year-old left-handed postgraduate university student who describes a profound, lifelong difficulty in recognizing people by their faces. She reports relying heavily on featural cues such as hair color and style, eyeglasses, and eyebrows to recognize new acquaintances. C also has difficulty recognizing characters in television programs, but after repeated viewings she can learn to identify a few key individuals. In the context of our investigations, C was only able to recognize us with any reliability after six months of meetings. On the basis of C's educational achievements, we estimated her IQ to be above average. (She could not be tested on standardized intelligence scales because she was already highly familiar with them through her postgraduate training in psychology.)

Behavioral Results

We examined C by using a battery of face- and object-perception tests. On the Benton Face Recognition Test [4], which requires participants to select a target face from a set of distractor faces, C scored 36/54. This score indicates a severe impairment of face recognition, and is equivalent to performance of individuals with acquired prosopagnosia [5, 6]. By contrast, previously reported cases of developmental prosopagnosia have scored within or close to the normal range on this test [7–10]. Interestingly, C was always correct when the test face and the correct target face were identical but made errors when the test face was shown from a different perspective. This suggests that C uses a strategy of feature matching when making judgments about facial identity, an approach that is ineffective for faces depicted from different angles (for discussion, see [11]).

We also explored C's ability to recognize faces configurally. It is widely accepted that face perception involves configural analysis (for review, see [12]). A striking demonstration of such configural processing arises when the top half of one face is presented with the bottom half of another to create a composite face. Normal participants are slower to identify either half when the segments are aligned than when they are misaligned. These results suggest that aligned composites are fused automatically and therefore perceived as a whole face rather than as two different halves [13]. We had C identify either the top or bottom half of composite stimuli constructed from faces that were familiar to her. She was significantly slower to identify either half when the segments were aligned than when they were misaligned (aligned mean reaction time [RT]: 496 ms; misaligned mean RT: 467 ms; $t(279) = 2.01$, $p < 0.05$). On the basis of these findings, we can conclude that C uses normal configural processing for familiar faces.

We also examined C's ability to remember unfamiliar faces by using the face-memory subtest from the Wechsler Memory Scale–Third Edition. C was asked to remember 24 unfamiliar target faces that were shown for 2 s each. She was then immediately shown 48 faces, half of which had been presented in the study phase, and asked to decide whether each face belonged to the original set. C scored 25/48 correct, more than 2 standard deviations (SDs) below the normal level for her age and not significantly different from chance.

*Correspondence: mark.williams@maccs.mq.edu.au

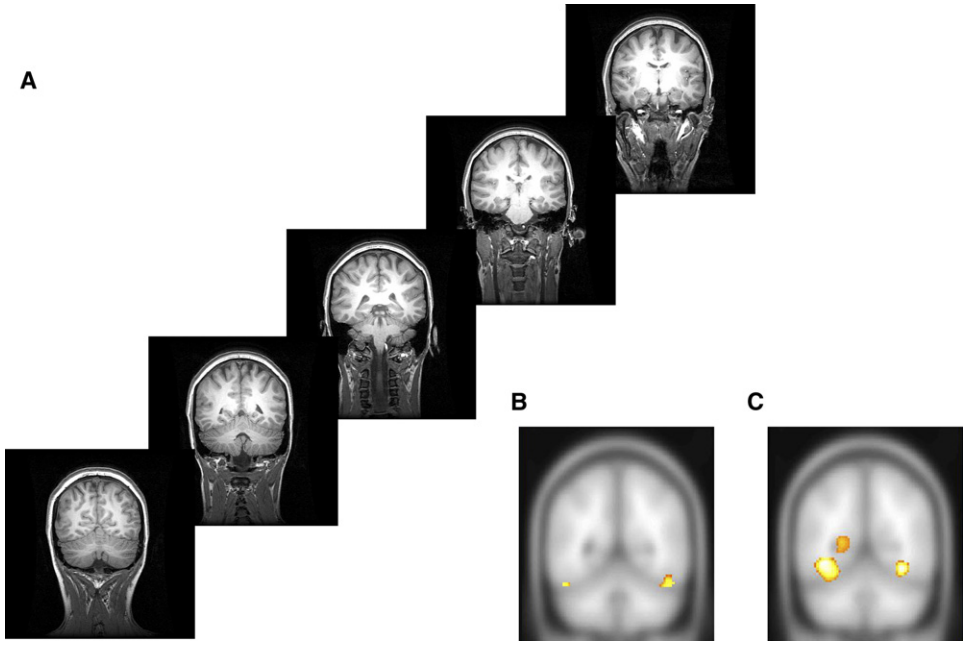

Figure 1. Structural- and Functional-MR Brain Images from "C," Who Has Prosopamnesia

(A) High-resolution structural-MR images. Detailed radiological inspection of the images in all three slice planes failed to reveal any structural lesion.

(B) Statistical parametric maps obtained from the localizer run, showing significant face-stimuli-specific bilateral activity in the fusiform gyrus.

(C) Statistical parametric maps obtained from the localizer run, showing significant place-stimuli-specific bilateral activity in the parahippocampal gyrus.

Taken together, our behavioral data suggest that C's deficit involves encoding or recognizing unfamiliar faces in particular, rather than in face perception per se. If this is correct, then C should be relatively good at recognizing familiar faces and in distinguishing them from unfamiliar faces. To examine this prediction, we asked C to list television and movie celebrities whom she felt she could recognize by face alone. We paired each of 42 of these familiar faces (examples included Kylie Minogue, Madonna, Jennifer Aniston, and Brad Pitt) with a single foil (an unknown person of the same sex and age, and with similar hair style and color, complexion, etc.) and asked C to indicate which of the two faces was familiar. She scored 90.5% correct in this task, indicating that her ability to discriminate between familiar and unfamiliar faces is relatively good.

From these initial tests, we hypothesized that C's face-perception deficit is specific to establishing stable representations of new (i.e., previously unfamiliar) faces. Her performance on the composite-faces task suggests that she processes faces configurally, and her ability to discriminate familiar from unfamiliar faces suggests that with repeated exposure she can acquire facial representations. Clearly, however, her ability to learn new faces is highly abnormal.

As a final check on the specificity of C's impairment for unfamiliar faces, we examined her ability to perceive nonface objects by using the Birmingham object-recognition battery (BORB). C was above average on all of the subtests, suggesting that her ability to recognize simple and complex nonface objects is intact (length: 27/30; size: 29/30; orientation: 28/30; position of gap: 40/40; overlapping figures: ceiling; minimal feature: 25/25; foreshortened: 25/25; object decision [hard version]: 27/32; item: 32/32; association: 30/30; and picture naming: 34/35). She also performed above average (32/32 correct) on the embedded-figures test [4], in which participants search for a target shape within a complex figure, and had normal color vision as assessed by the Ishihara test for color blindness [14].

In summary, our behavioral tests demonstrate that C has a highly specific impairment in learning new faces in the context of intact processing of familiar faces and other objects. To investigate the neural correlates of C's unusual deficit, we conducted a series of structural- and functional-MRI studies. We focused in particular on the integrity of the fusiform face area (FFA), a region of the fusiform gyrus known to be involved in face processing [15–17].

Neuroimaging Results

We first acquired high-resolution structural magnetic resonance (MR) images of C's brain (Figure 1A), because structural lesions of the fusiform gyrus have previously been reported to cause prosopamnesia [1]. A thorough, slice-by-slice radiological examination of these images failed to reveal any structural abnormalities. We also examined physiological activity within the fusiform area and elsewhere by using functional magnetic resonance imaging (fMRI). As outlined in detail below, these investigations revealed the expected pattern of increased activity in the FFA during presentation of faces compared with presentation of places (Figures 1B and 1C).

Defining Regions of Interest for Faces and Places

We localized the FFA in C and a group of normal controls by contrasting the blood-oxygen-dependent

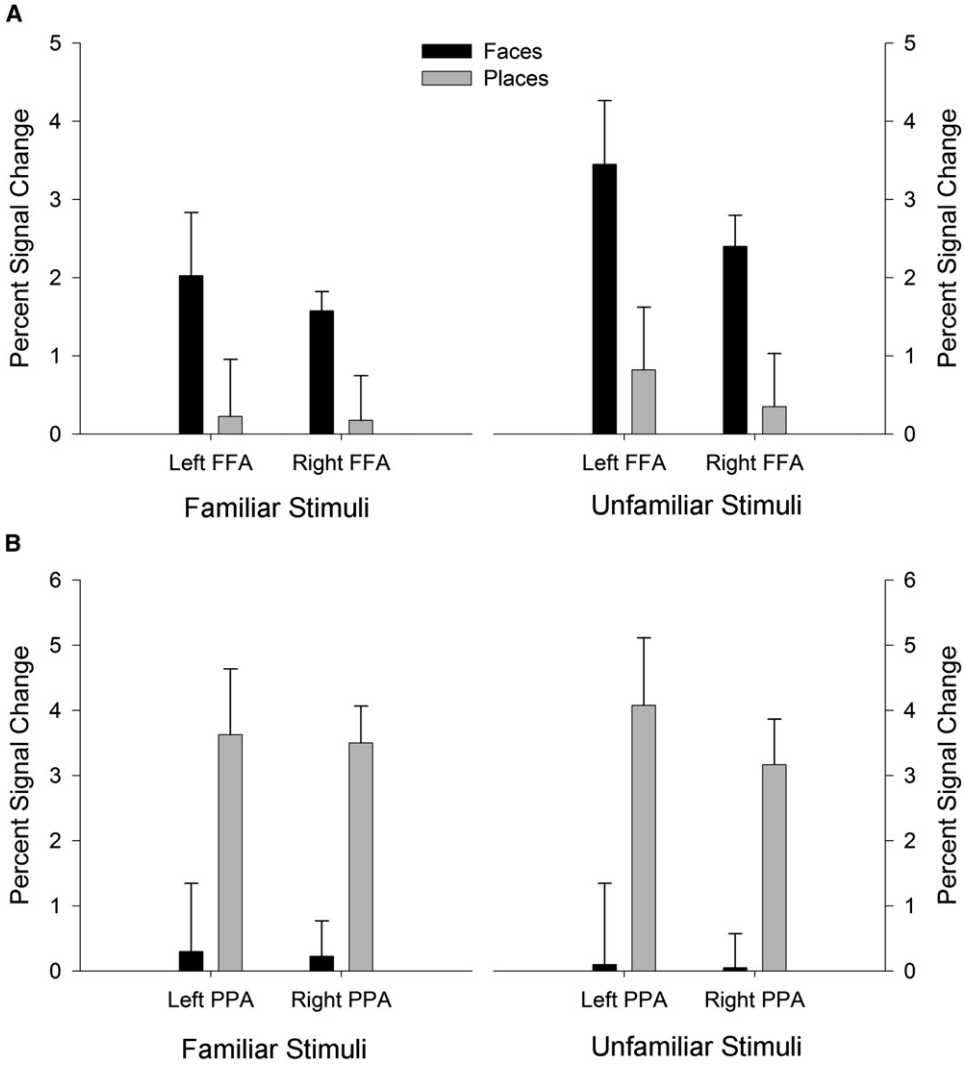

Figure 2. Results of the ROI Analyses on the FFA and PPA for the First Presentation of Familiar and Unfamiliar Faces and Places

(A) BOLD signal change in the FFA (± one standard error), plotted separately for the familiar and unfamiliar face conditions.

(B) Graph shows BOLD signal change in the PPA (± one standard error), plotted separately for the familiar and unfamiliar place conditions.

response (BOLD) when participants viewed faces versus places. The place stimuli (i.e., images of houses and buildings) were chosen for comparison because these are known to activate a region of the parahippocampal gyrus (the parahippocampal place area; PPA) [18]. We defined regions of interest (ROIs) in the FFA and PPA by using a conventional blocked design and then examined activity within the ROIs in response to repeated presentations of familiar and unfamiliar faces and places.

In the localizer task, C viewed alternating blocks of familiar faces and familiar places. A t test comparing the face minus place epochs revealed significant bilateral activity in the fusiform gyrus (left peak x y z, 46 −46 −22, $t = 7.68$, $p < 0.001$; right peak x y z, −56 −64 −18, $t = 8.12$, $p < 0.001$, Figure 1B). The reverse contrast for place minus face epochs revealed significant bilateral activity in the parahippocampal gyrus (left peak x y z, 32 −56 −12, $t = 11.13$, $p < 0.001$; right peak x y z, −40 −54 −8, $t = 11.41$, $p < 0.001$, Figure 1C). As with normal participants, C's FFA and PPA show a selective increase in activity during exposure to faces and places, respectively (Figure 2).

The Repetition-Suppression Effect for Familiar and Unfamiliar Faces and Places

Previous fMRI studies have shown that neural responses to objects, places, and faces are attenuated across repeated presentations of the same stimuli, an effect known as repetition suppression [19–22]. Evidence from both monkeys and humans suggests that this effect is localized to regions specifically tuned to stimuli belonging to the repeated category [18–28], implying a possible role for repetition suppression in perceptual learning [24]. Previous studies have found that repetition suppression is sometimes lateralized to one cerebral hemisphere [20, 21, 29, 30]. Because damage to the right fusiform gyrus alone can cause acquired prosopagnosia [5, 6], we predicted that for C, activity in the right FFA should decrease in response to repetition of familiar faces, but not in response to repetition of unfamiliar faces, consistent with her behavioral difficulties in learning new faces.

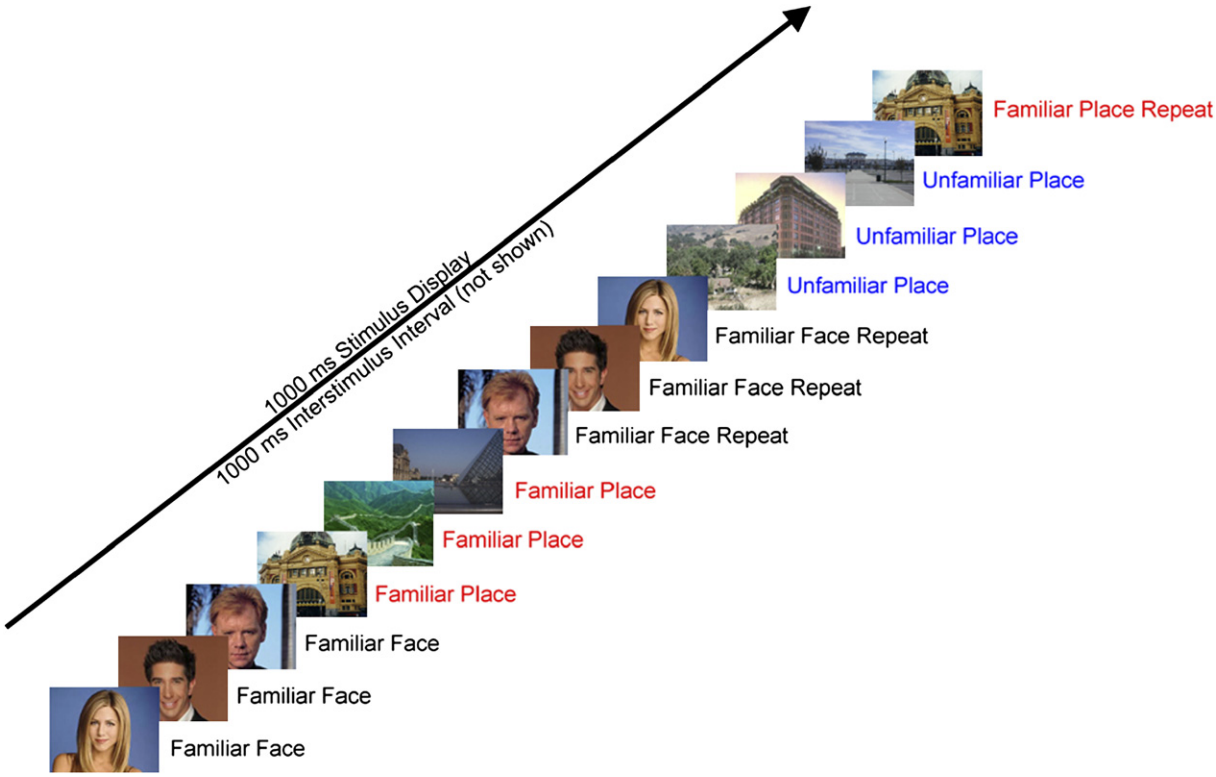

Figure 3. Typical Sequence of Displays in the Repetition Task

In this example, two familiar faces and two familiar places are repeated. During the experiment, C indicated via a button box whether the stimulus was familiar or unfamiliar (637/640 correct responses).

We presented familiar and unfamiliar faces and places in an event-related design (see Supplemental Experimental Procedures in the Supplemental Data available online). Each image was repeated once after an average delay of 29 s (SD = 14.25; Figure 3; see Supplemental Experimental Procedures). As predicted, ROI analyses revealed a significant decrease in activity within the right FFA for repetitions of familiar faces (right peak, $t = 3.37$, $p < 0.001$, Figure 4A). Critically, however, the same comparison for unfamiliar faces revealed no significant change in activity upon repetition (Figure 4A). Moreover, analyses conducted on the functionally defined PPA revealed significant attenuation for repetitions of *both* familiar and unfamiliar places (familiar places: right peak, $t = 3.60$, $p < 0.001$; unfamiliar places: left peak, $t = 6.29$, $p < 0.001$; right peak, $t = 7.81$, $p < 0.001$, Figure 4B). Thus, C shows normal repetition suppression for both familiar and unfamiliar places, and for familiar faces, but she shows no such effect within the FFA for unfamiliar faces, consistent with her behavioral deficit for these novel stimuli.

Comparison with Normal Controls

To verify that C's fMRI results are indeed unusual, we tested four matched control participants (3 left-handed) with identical protocols. Critically, every control participant showed a robust repetition-suppression effect within the right FFA for *both* familiar faces (control 1: $t = 3.86$, $p < 0.001$; control 2: $t = 2.83$, $p < 0.002$; control 3: $t = 2.99$, $p < 0.001$; control 4: $t = 3.21$, $p < 0.001$) and unfamiliar faces (control 1: $t = 4.42$, $p < 0.001$; control 2: $t = 2.61$, $p < 0.005$; control 3: $t = 4.24$, $p < 0.001$; control 4: $t = 3.54$, $p < 0.001$). In addition, every control participant showed significant repetition suppression within the right PPA for both familiar places (control 1: $t = 3.67$, $p < 0.001$; control 2: $t = 4.40$, $p < 0.001$; control 3: $t = 4.82$, $p < 0.001$; control 4: $t = 2.66$, $p < 0.004$) and unfamiliar places (control 1: $t = 4.69$, $p < 0.001$; control 2: $t = 4.63$, $p < 0.001$; control 3: $t = 5.78$, $p < 0.001$; control 4: $t = 2.87$, $p < 0.002$; Figure 4; see Figure S2 for more details), consistent with previous investigations [28–35]. There was also a significant difference between magnitude of C's repetition-suppression effect and each of the control subjects in the unfamiliar-faces condition (C versus control 1: $t = 3.79$, $p < 0.01$; C versus control 2: $t = 3.24$, $p < 0.01$; C versus control 3: $t = 5.62$, $p < 0.01$; C versus control 4: $t = 4.46$, $p < 0.01$).

In summary, each of the four matched controls showed reliable repetition suppression for both familiar and unfamiliar faces and places. We can thus be confident that in C, the absence of attenuated activity in the FFA across repetitions of unfamiliar faces is a highly specific and abnormal effect.

These results demonstrate that the normal mechanisms of neural adaptation to repeated unfamiliar faces are selectively impaired in C. This fits with C's severe and circumscribed problems in learning new faces. By contrast, we observed significant attenuation within the same functionally defined region to repeated presentations of *familiar* faces and within the PPA to repeated familiar and unfamiliar places. We can thus rule out any generalized impairment of neural adaptation in C. Our findings are broadly consistent with those of a previous

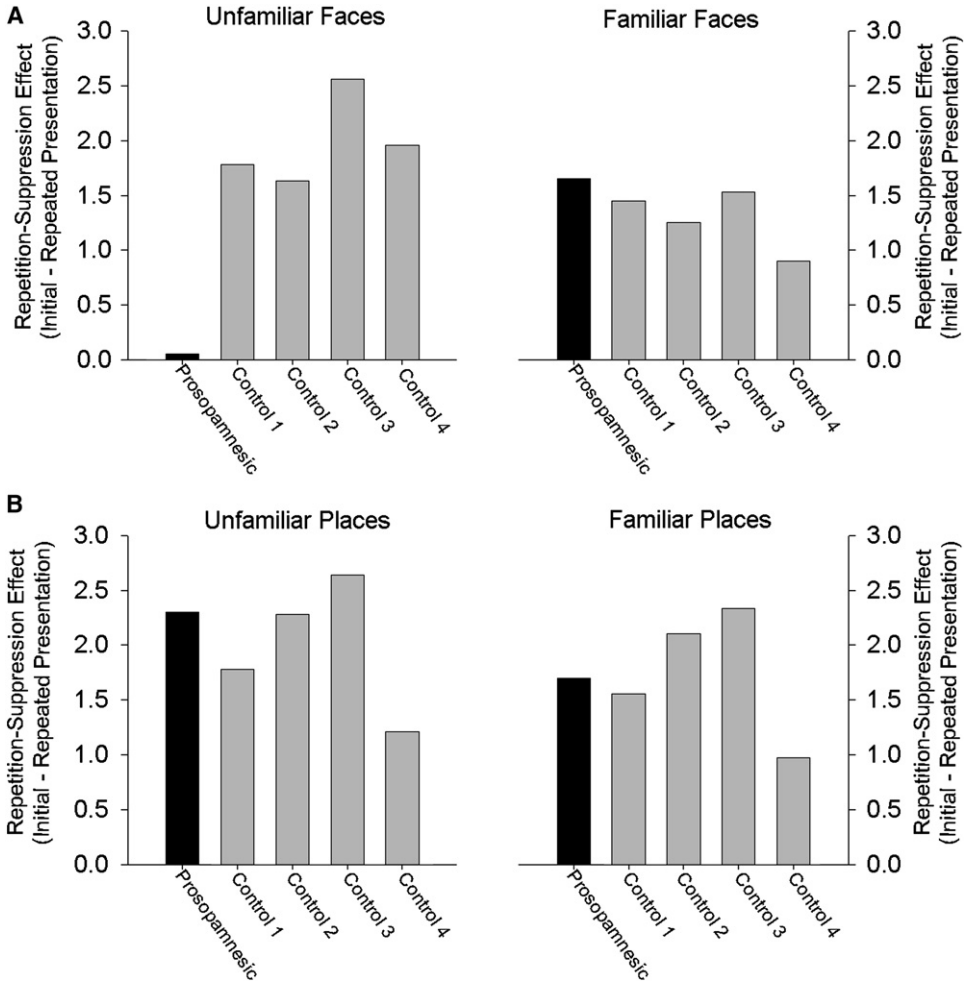

Figure 4. Results of the ROI Analyses on the Right FFA and PPA for the Manipulation of Repeated Familiar and Unfamiliar Faces and Places

(A) Difference in BOLD signal change in the right FFA for initial minus repeated presentation, as a function of familiar- and unfamiliar-face conditions.

(B) Difference in BOLD signal change in the right PPA for initial minus repeated presentation, as a function of familiar- and unfamiliar-place conditions.

study of acquired prosopagnosia [32], in which repetition suppression within the fusiform gyrus was absent for repeated (unfamiliar) face stimuli. Our results extend this finding by showing a circumscribed deficit in learning new faces associated with a failure of neural adaptation to unfamiliar face images in the context of normal adaptation to familiar faces.

For C, initial exposure to an unfamiliar face, even over multiple encoding episodes, is not sufficient to support a persistent memory trace. It may be that enduring face representations are slow to form or are degraded in quality, or they may decay rapidly following normal encoding. The current findings do not allow us to distinguish between these possibilities. What we can say with certainty, however, is that when a previously unfamiliar face is seen for a second time just a few seconds after an initial exposure, C's FFA responds as if that face is entirely novel. Our behavioral observations suggest that a stable representation is finally consolidated after many repetitions, because C can eventually learn to recognize some faces, but the exact time course of this learning effect remains unclear. In C, a severe but highly specific impairment in learning new faces is accompanied by an abnormal and equally specific neural response in the FFA. Thus, repetition suppression has revealed a neural marker for the striking behavioral anomaly observed in our prosopamnesic case.

Experimental Procedures

Details of the experimental procedures and analyses are given in the Supplemental Data. Face photographs of 50 individuals (25 familiar, 25 unfamiliar) and 50 places (25 familiar, 25 unfamiliar) were selected to match as closely as possible in overall area. Preprocessing and data analysis were performed with SPM2 (Wellcome Department of Imaging Neuroscience; http://www.fil.ion.ucl.ac.uk/spm/).

Supplemental Data

Experimental Procedures and two figures are available at http://www.current-biology.com/cgi/content/full/17/14/1259/DC1/.

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